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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/667,796	09/22/2000	Wayne R. Curtis	99-2175	9738

7590 04/10/2003

Intellectual Property Office
The Pennsylvania State University
113 Technology Center
University Park, PA 16802

EXAMINER
FOX, DAVID T

ART UNIT	PAPER NUMBER
1638	15

DATE MAILED: 04/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/667,796	Curtis
Examiner	**Group Art Unit**
FOX	1638

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P riod f r Reply -3-

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 10/10/02 & 1/24/03.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☑ Claim(s) 1-12 and 15-20 is/are pending in the application.

Of the above claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☑ Claim(s) 1-12 and 15-20 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notic of Informal Patent Application, PTO-152

☐ Other _____

Office Acti n Summary

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10 October 2002 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-12 and 15-20 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a method for transforming dicotyledonous cells or hairy root cultures via the utilization of an auxotropic strain of Agrobacterium tumefaciens containing a gene encoding a heterologous protein of interest, does not reasonably provide enablement for claims broadly drawn to Agrobacterium-mediated transformation of monocotyledonous cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, as stated in the last Office action for claims 1-20.

Applicant's submission of Bakkeren et al is noted. This reference teaches the use of agroinfection with viral sequences in order to obtain monocot transformation by *Agrobacterium*, which technique was not taught in the instant specification. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere

germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-12 and 15-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, part ii), lines 3-4, is indefinite in the recitation of "to the plant tissue sample" as the relationship of this phrase to the rest of the claim elements is unclear. Deletion of the phrase would obviate this rejection. Dependent claims are included in the rejection.

Claims 18-19 are indefinite in their dependence upon cancelled claims 14 and 13, respectively.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-7, 11, 16 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Gomord et al.

The claims are broadly drawn to a method for utilizing a bioreactor for culturing a liquid suspension culture of dicotyledonous cells including tobacco cells, inoculation of the plant cells with *Agrobacterium tumefaciens* containing a gene encoding a polypeptide or protein of interest, followed by culture of the inoculated plant cells in a liquid medium for expression of the recombinant polypeptide, wherein conditions including protein expression level are monitored prior to final protein isolation, wherein the bioreactor has at least 50 ml liquid medium, wherein the plant cells and *Agrobacterium* are cultured together for 1-4 days, and wherein the pH of the culture medium is between 4.9-6.1.

Gomord et al teach the culture of 150 mL of tobacco suspension cells, their inoculation via 2-3 day coculture with *Agrobacterium tumefaciens* containing a heterologous gene encoding a lectin protein, continued liquid suspension culture of the transformed tobacco cells for two weeks, monitoring of protein expression levels via detection of lectin levels 1 day after transformation, followed by final protein isolation 2 or three days later, wherein high levels of recombinant protein were observed (see, e.g., page 155, bottom paragraph; page 156, first full paragraph; page 158, sections 3.2 and 3.3.1; page 159, Figure 1 and section 3.3.3; page 160, Figure 2, second paragraph of Legend). The pH of the buffered MS medium would inherently have been between 4.9 and 6.1, which are known in the art as typical plant culture parameters.

Claims 1-3, 5-8, 11-12 and 15-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gomord et al taken with Hiei et al.

The claims are broadly drawn to the use of a bioreactor to transform cultured dicotyledonous or monocotyledonous plant cells, including corn cells, with *Agrobacterium tumefaciens* containing a gene encoding a protein of interest including an enzyme, wherein the *Agrobacterium* is added at between 7 and 14 days of plant culture or at a particular plant biomass concentration, wherein an inducer such as acetosyringone is used, and wherein 100 mg of recombinant protein per 100 liters is produced.

Gomord et al teach a method for inoculating plant cells with *Agrobacterium* as discussed above, and suggest the use of the method for the production of a wide range of heterologous proteins in a wide range of plant species (see, e.g., page v, top and bottom paragraphs of Preface).

Gomord et al do not teach monocot transformation, the use of acetosyringone to activate the *Agrobacterium*, the particular age of the cultured cells to be inoculated, or the particular level of protein production claimed.

Hiei et al teach the use of acetosyringone to pre-culture the *Agrobacterium*, as well as the use of acetosyringone in the bacteria/plant co-culture culture medium, to incolate monocotyledonous suspension cells including rice and corn, wherein the heterologous gene encoded the enzyme beta-glucuronidase (see, e.g., column 7, lines 29-49; column 8, lines 1-12; column 9, lines 30-62; column 11, lines 25-50; column 17, lines 62-67; column 18, lines 17-25 and 60-65; column 19, lines 53-60; column 20, Table 11).

It would have been obvious to one of ordinary skill in the art to utilize the method for producing heterologous proteins in liquid culture via *Agrobacterium* inoculation as taught by Gomord et al, and to modify that method by incorporating monocot cells and acetosyringone activation as taught by Hiei et al, given the broad applicability of the technique as suggested by Gomord et al. Choice of particular pH, culture age prior to transformation, heterologous protein gene, and level of protein production would have been the optimization of process parameters.

Claims 1-3, 5-7, 9-11 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gomord et al taken with Sastry et al (abstract relied upon).

The claims are broadly drawn to the use of an auxotrophic *Agrobacterium* strain for inoculation of a liquid suspension of plant cells for the production of a heterologous protein.

The teachings of Gomord et al are summarized above. Gomord et al do not teach the use of an auxotrophic bacterial strain.

Sastry et al teach the advantages of using an auxotrophic *Agrobacterium* strain, such as the tryptophan (-) containing the *ctu* mutation, for the containment of engineered bacterial strains.

It would have been obvious to one of ordinary skill in the art to utilize the method for producing heterologous proteins in liquid culture via *Agrobacterium* inoculation as taught by Gomord et al, and to modify that method by incorporating auxotrophic bacterial strains as taught by Sastry et al, given the broad applicability of the technique as suggested by Gomord et al and the advantages of auxotrophs taught by Sastry et al. Choice of particular pH, culture age prior to

transformation, heterologous protein gene, and level of protein production would have been the optimization of process parameters.

Claims 1-2, 4-7, 11-12 and 15-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gomord et al taken with Wongsamuth et al.

The claims are broadly drawn to the use of *Agrobacterium rhizogenes* to produce hairy roots for plant tissue culture-mediated production of heterolgous proteins including antibodies.

The teachings of Gomord et al are summarized above. Gomord et al do not teach the use of *A. rhizogenes* or antibody production.

Wongsamuth et al teach the wide applicability of *A. rhizogenes*-induced hairy root culture for the production of desired compounds, and the use of cultured hairy roots at pH 5.7 to produce antibodies, wherein the bioreactor-cultured roots had the advantage of long-term stability and high levels of antibody production (see, e.g., page 402, column 2, first and second full paragraphs; page 403, column 1; page 404, paragraph bridging the columns; paragraph bridging pages 406 and 407; page 411, column 2, first full paragraph).

It would have been obvious to one of ordinary skill in the art to utilize the method for producing heterologous proteins in liquid culture via *Agrobacterium* inoculation as taught by Gomord et al, and to modify that method by incorporating *A. rhizogenes* strains and antibody-encoding genes as taught by Wongsamuth et al, given the broad applicability of the technique as suggested by Gomord et al and the advantages of hairy root culture in bioreactors taught by Wongsamuth et al. Choice of particular pH, culture age prior to transformation, sequence of

introducing *A. rhizogenes* to plant cells including the use of *A. rhizogenes* containing the transgene to inoculate untransformed cells, heterologous protein gene, and level of protein production would have been the optimization of process parameters.

Claims 1-18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al, as stated in the last Office action.

Claims 1, 13, 19 and 20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al taken with Baszczynski et al, as stated in the last Office action.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

April 5, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180 1638